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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,152	02/18/2005	Roger Alberto	1582 WO/US	5284
7590 Mallinckrodt Inc. 675 McDonnell Boulevard PO Box 5840 Hazelwood, MO 63134			EXAMINER GROSS, CHRISTOPHER M	
			ART UNIT 1639	PAPER NUMBER
			MAIL DATE 11/09/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/525,152

Applicant(s)

ALBERTO ET AL.

Examiner

CHRISTOPHER M. GROSS

Art Unit

1639

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/29/2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17, 20-24, 28 and 32-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17, 20-24, 28 and 32-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/003)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Responsive to communications entered 6/29/2009. Claims 15-17,20-24,28,32-36 are pending. Claims 15-17,20-24,28,32-36 are under consideration.

Priority

The present application, filed 2/18/2005 claims priority as a 371 of PCT/US03/27665 filed 09/02/2003 and foreign priority to European application (EPO) 02078743.8 filed 09/03/2002.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Applicant's arguments on p 7 of the remarks entered 6/29/2009 are deemed persuasive and accordingly Harry Kim of PCT legal at the Office has retrieved the foreign priority document which is being entered into the record.

Response to Arguments

While the examiner does not find support for the genus of solid phase bound organic conjugates directly attached to the support set forth in claims 15 and 20 in the European application, the examiner acknowledges applicant's amendments to claims 15 and 20 find support in PCT/US03/27665 and thus claims 15-17,20-24,28,32-36 are afforded a priority date of 9/2/2003.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claims 15-17,20-24,28,32-36 under 35 U.S.C. 102(b) as being anticipated by **Mundwiler et al** (2004 Bioconjugate Chem. 15:195-202; public

availability date on the Web 12/16/2003) is hereby withdrawn in view of applicant's amendments.

New Claim Rejection(s) – Necessitated by Amendment

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-17,20,21,24,28,32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gustavson et al** (US Patent 6022966) in view of **Ngu et al** (1997 Tetrahedron Letters 38:973-976).

The claimed subject matter per claim 15 is drawn to a solid phase organic conjugate represented by formula (I)

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wherein the sphere is a solid phase support;

C is a carbon atom;

R4 and R5 are independently selected from the group consisting of H, aliphatic substituents, aromatic substituents, RO, RS and (R)₂N, wherein R is an aliphatic or aryl group;

and

each of R1 and R2 is independently a metal coordinating group, a non-coordinating organic group, a metal coordinating group derivatized with a biologically active molecule, or a non-coordinating organic group derivatized with a biologically active molecule, wherein at least one of R1, and R2 is independently selected from the group consisting of [R3-picolyl, R3-imidazole or an R3-amine]

wherein R3 is directly attached to the tertiary amine or is an aliphatic chain containing between 1 and 3 carbons directly attached to the tertiary amine.

Claims 16,17,20,21,24,28,32-34 constitute variations of the above

Gustavson et al teach, throughout the document and especially the abstract and patent claim 7, compounds and kits for pre-targeted delivery of diagnostic and therapeutic agents using biotin and chelated metals such as Technetium-99m. As illustrated in column 57, in one embodiment, said compounds are prepared starting with Boc-ethylenediamine to form biotinamidoethylene diamine, which reads on each of claims 15 and 20 (in part) when R1 =CH₂CH₂NH₂; R2 is biotin (a non-coordinating organic group derivatized with a biologically active molecule); R3= CH₂CH₂

Said biotin (elected species) reads on claims 28 and 33 as well as the pharmaceutically active small molecule of claims 16 and 32.

In column 99 line 22 and column 96 line 65, Gustavson et al teach kits including sterile containers and vessels, further reading on the container and kit of claim 20 as well as claim 21.

Please note in column 61, Gustavson et al also teach biotinamidopentyl[di]amine as well, a homolog of the presently claimed organic conjugates, and according to MPEP 2144.09: compounds which are homologs (*compounds differing regularly by the*

successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Absent evidence to the contrary, the biotinamidopentyl[di]amines of Gustavson et al would have similar properties to the biotinamidopropyl diamines claimed, for instance.

Gustavson et al do not teach: a solid phase support such as a hybrid of polyethylene glycol and polystyrene such as set forth in claims 15,17,20,34; a facility for filtration as set forth in claim 24.

Ngu et al teach, throughout the document and especially the title and abstract, preparation of acid-labile resins bearing halide linkers applied toward solid phase organic synthesis. In particular, Ngu et al teach in schemes 1 and 2, the conversion of TentaGel S AC resin bearing a Wang handle (a solid support composed of a hybrid of polyethylene glycol and polystyrene; elected species; claims 15,17,20,34) to a halide. Said solid phase organic synthesis inherently includes a facility for filtration (following cleavage), reading on claim 24. Under this scenario, R₄=R₅=H in claims 15 and 20.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use the halide resin of Ngu et al to form various derivatives of biotinamidoethylene diamine per Gustavson et al.

One of ordinary skill in the art would have been motivated to use the halide resin of Ngu et al to form various derivatives of biotinamidoethylene diamine per Gustavson et al because it provides the means to perform combinatorial organic synthesis - an

important tool for drug discovery – with desirably high yields and purity, as noted by Ngu et al in the first paragraphs on each of p 973,976.

One of ordinary skill in the art would have had a reasonable expectation of success in transferring the solution phase chemistry of Gustavson et al to the solid phase per Ngu et al because both Boc-ethylenediamine and biotinamidoethylene diamine bear amine functional groups well suited to toward immunization using the same chemistry as shown in scheme 2 of Ngu et al.

Claims 22-23,35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gustavson et al** (US Patent 6022966) in view of **Ngu et al** (1997 Tetrahedron Letters 38:973-976) as applied to claims 15-17,20,21,24,28,32-34 above, and further in view of **Alberto et al** (1998 JACS 120:7987-7988 – IDS entry 4/27/2005).

Gustavson et al in view of Ngu et al is relied on as above.

Gustavson et al in view of Ngu et al do not teach biomolecule labeling with a solution of [$^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3$] $^+$, such as set forth in claims 22,35-36 or the reagents for the preparation of $[\text{M}(\text{OH}_2)_3(\text{CO})_3]^+$, as set forth in claim 23.

Alberto et al, teach throughout the document and especially scheme 1, a solution of and the reagents necessary for the preparation of [$^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3$] $^+$ for labeling biomolecules, reading on claims 22-23,35-36.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to place a container of reagents for the preparation of a solution of $[\text{M}(\text{OH}_2)_3(\text{CO})_3]^+$ or a solution of [$^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3$] $^+$ itself

per Alberto et al next to the biotinamidoethylene diamine loaded on the TentaGel resin per Gustavson et al in view of Ngu et al.

One of ordinary skill in the art would have been motivated to place a container of reagents for the preparation of a solution of $[M(OH_2)_3(CO)_3]^+$ or a solution of $[^{99m}Tc(OH_2)_3(CO)_3]^+$ itself per Alberto et al next to the biotinamidoethylene diamine loaded on the TentaGel resin per Gustavson et al in view of Ngu et al because (i) the desirable kinetic stability of the d^6 complexes thus prepared is well suited for labeling biomolecules according to Alberto et al on p 7988 left column second paragraph and (ii) ^{99m}Tc , in particular as a radionuclide, is inexpensive and readily available in any hospital, according to Alberto et al on p 7988 left column second paragraph. Notably, Gustavson et al similarly envision ^{99m}Tc biotin labeling in column 8 line 34-42.

One of ordinary skill in the art would have had a reasonable expectation of success in placing a container of reagents for the preparation of a solution of $[M(OH_2)_3(CO)_3]^+$ or a solution of $[^{99m}Tc(OH_2)_3(CO)_3]^+$ itself per Alberto et al next to the biotinamidoethylene diamine loaded on the TentaGel resin per Gustavson et al in view of Ngu et al because kits including separate flasks and containers have been successfully used in the art for some time.

In conclusion, the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and was as a whole, prima facie obvious.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571 272 0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

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/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1639